A HINDBRAIN DOPAMINERGIC NEURAL CIRCUIT PREVENTS WEIGHT GAIN BY REINFORCING FOOD SATIATION

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Background: The dopaminergic (DA) neural circuits are established in differential control of various reward processes. However, the circuitry mechanism that directly mediates foraging and feeding behavior per se is unknown.

Materials/Methods: Transgenetic mice: Slc6a3-Cre mice, Drd1-Cre mice, and Drd1-lox/lox mice. The mice will be performed with Stereotaxic Viral Injections, Double Retrograde Labeling, Ablation of DAcVTA Neurons projecting to the LPBN, Optogenetics, Drug Administration, Food Intake test, Measurement of locomotor activities, In vitro Electrophysiology, In vivo Tetrode Recording, and histology.

Results: 1. A subpopulation of DA neurons within the caudal VTA (cVTA) exclusively projects to the D1R neurons within the lateral PBN (LPBN). 2. Genetic stimulation of the DAVTA-PBN neurons or downstream D1RPBN neurons potently suppresses hunger-induced feeding, whereas suppression of these neurons causes hyperphagic effects. 3. The LPBN-projecting DAcVTA neurons encode meal termination. 4. Methylphenidate (MPH) mediates hypophagia and body weight loss through the cVTADA→LPBNDRD1 circuit.

Conclusions: Our study illuminates a hindbrain DAergic circuit that controls feeding through dynamic regulation in satiety response and meal structure.

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